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☐	L25	WO-200215913$.did.	1
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☐	L23	L22 and polyanionic polymer	3
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☐	L4	l3 or l2 or l1	39
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☐ 1. Document ID: US 6756362 B2

L12: Entry 1 of 9 File: USPT Jun 29, 2004

DOCUMENT-IDENTIFIER: US 6756362 B2
TITLE: Methods and compositions based on inhibition of cell invasion and fibrosis by anionic polymers

Detailed Description Text (53):
The invention provides for application of an inhibitory composition or inhibitory-adhesive composition by surgical procedures. The inhibitory anionic polymer or inhibitory-adhesive may be applied-to a surgical wound. The anionic polymer or inhibitory-adhesive may be directly applied to sites of tissue injury, or to coat an entire organ or to close a surgical incision. Where suitable, administration of the inhibitory anionic polymer or inhibitory-adhesive composition may be made by orthroscopic procedures.

Detailed Description Text (124):
PC-12 cells primed with NGF were plated in 96-well plates. Test solutions were added to the wells and the cells were scored 2 days later as (+) if neurites of at least two cell bodies diameter in length were present on the majority of the cells, and (-) if no or only short processes were present. Complete dose-response curves were generated for each test compound and the results were expressed as IC.sub.100 (g/ml), i.e., the minimum concentration at which the compound caused 100% inhibition-of neurite outgrowth (Table 10). The lack of toxicity by each compound tested was confirmed as follows: microscopically, no evidence of cell death and detachment was seen; cells did not stain positive for trypan blue; and removal of the inhibitory compound from the culture medium resulted in neurite outgrowth. The compounds tested included GAGs (heparin, dermatan sulfate, chondroitin sulfate A, keratan sulfate and hyaluronic acid), sulfated carbohydrate polymers (dextran sulfate and pentosan polysulfate), and another polyanionic polymer (e.g., alginic acid).

Detailed Description Text (125):
A compound's relative inhibitory potency in vitro appeared to positively correlate with sulfur content. The contribution of the sulfur functional group is most clearly demonstrated by comparing the activity of dextran sulfate to that of dextran. The sulfur found as sulfate on the GAGs most likely affects cell invasion by anionic charge density. To test this hypothesis, we used alginic acid (alginate), a polyanionic polymer with a negative charge due only to carboxyl groups. As shown in Table 10, alginic acid also inhibits cell migration. These results indicate that an active inhibitory element of a given polymer is its anionic (negative) charge density.

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw

☐ 2. Document ID: US 6417173 B1

L12: Entry 2 of 9 File: USPT Jul 9, 2002

DOCUMENT-IDENTIFIER: US 6417173 B1
TITLE: Methods and compositions based on inhibition of cell invasion and fibrosis by anionic polymers

Drawing Description Text (64):
The invention provides for application of an inhibitory composition or inhibitory-adhesive composition by surgical procedures. The inhibitory anionic polymer or inhibitory-adhesive may be applied to a surgical wound. The anionic polymer or inhibitory-adhesive may be directly applied to sites of tissue injury, or to coat an entire organ or to close a surgical incision. Where suitable, administration of the inhibitory anionic polymer or inhibitory-adhesive composition may be made by orthroscopic procedures.

Detailed Description Text (71):
PC-12 cells primed with NGF were plated in 96-well plates. Test solutions were added to the wells and the cells were scored 2 days later as (+) if neurites of at least two cell bodies diameter in length were present on the majority of the cells, and (-) if no or only short processes were present. Complete dose-response curves were generated for each test compound and the results were expressed as IC.sub.100 (g/ml), i.e., the minimum concentration at which the compound caused 100% inhibition of neurite outgrowth (Table 10). The lack of toxicity by each compound tested was confirmed as follows: microscopically, no evidence of cell death and detachment was seen; cells did not stain positive for trypan blue; and removal of the inhibitory compound from the culture medium resulted in neurite outgrowth. The compounds tested included GAGs (heparin, dermatan sulfate, chondroitin sulfate A, keratan sulfate and hyaluronic acid), sulfated carbohydrate polymers (dextran sulfate and pentosan polysulfate), and another polyanionic polymer (e.g., alginic acid).

Detailed Description Text (72):
A compound's relative inhibitory potency in vitro appeared to positively correlate with sulfur content. The contribution of the sulfur functional group is most clearly demonstrated by comparing the activity of dextran sulfate to that of dextran. The sulfur found as sulfate on the GAGs most likely affects cell invasion by anionic charge density. To test this hypothesis, we used alginic acid (alginate), a polyanionic polymer with a negative charge due only to carboxyl groups. As shown in Table 10, alginic acid also inhibits cell migration. These results indicate that an active inhibitory element of a given polymer is its anionic (negative) charge density.

☐ 3. Document ID: US 6127348 A

L12: Entry 3 of 9 File: USPT Oct 3, 2000

DOCUMENT-IDENTIFIER: US 6127348 A

TITLE: Methods and compositions based on inhibition of cell invasion and fibrosis by anionic polymers

Detailed Description Text (54):
The invention provides for application of an inhibitory composition or inhibitory-adhesive composition by surgical procedures. The inhibitory anionic polymer or inhibitory-adhesive may be applied to a surgical wound. The anionic polymer or inhibitory-adhesive may be directly applied to sites of tissue injury, or to coat an entire organ or to close a surgical incision. Where suitable, administration of the inhibitory anionic polymer or inhibitory-adhesive composition may be made by orthroscopic procedures.

Detailed Description Text (128):
PC-12 cells primed with NGF were plated in 96-well plates. Test solutions were added to the wells and the cells were scored 2 days later as (+) if neurites of at least two cell bodies diameter in length were present on the majority of the cells, and (-) if no or only short processes were present. Complete dose-response curves were generated for each test compound and the results were expressed as IC.sub.100 (g/ml), i.e., the minimum concentration at which the compound caused 100% inhibition of neurite outgrowth (Table 10). The lack of toxicity by each compound tested was confirmed as follows: microscopically, no evidence of cell death and detachment was seen; cells did not stain positive for trypan blue; and removal of the inhibitory compound from the culture medium resulted in neurite outgrowth. The compounds tested included GAGs (heparin, dermatan sulfate, chondroitin sulfate A, keratan splfate and hyaluronic acid), sulfated carbohydrate polymers (dextran sulfate and pentosan polysulfate), and another polyanionic polymer (e.g., alginic acid).

Detailed Description Text (129):
A compound's relative inhibitory potency in vitro appeared to positively correlate with sulfur content. The contribution of the sulfur functional group is most clearly demonstrated by comparing the activity of dextran sulfate to that of dextran. The sulfur found as sulfate on the GAGs most likely affects cell invasion by anionic charge density. To test this hypothesis, we used alginic acid (alginate), a polyanionic polymer with a negative charge due only to carboxyl groups. As shown in Table 10, alginic acid also inhibits cell migration. These results indicate that an active inhibitory element of a given polymer is its anionic (negative) charge density.

☐ 4. Document ID: US 6083930 A

L12: Entry 4 of 9 File: USPT Jul 4, 2000

DOCUMENT-IDENTIFIER: US 6083930 A
**** See image for Certificate of Correction ****
TITLE: Methods and compositions based on inhibition of cell invasion and fibrosis by anionic polymers

Detailed Description Text (55):
The invention provides for application of an inhibitory composition or inhibitory-adhesive composition by surgical procedures. The inhibitory anionic polymer or inhibitory-adhesive may be applied to a surgical wound. The anionic polymer or

inhibitory-adhesive may be directly applied to sites of tissue injury, or to coat an entire organ or to close a surgical incision. Where suitable, administration of the inhibitory anionic polymer or inhibitory-adhesive composition may be made by orthroscopic procedures.

Detailed Description Text (126):
PC-12 cells primed with NGF were plated in 96-well plates. Test solutions were added to the wells and the cells were scored 2 days later as (+) if neurites of at least two cell bodies diameter in length were present on the majority of the cells, and (-) if no or only short processes were present. Complete dose-response curves were generated for each test compound and the results were expressed as IC.sub.100 (g/ml), i.e., the minimum concentration at which the compound caused 100% inhibition of neurite outgrowth (Table 10). The lack of toxicity by each compound tested was confirmed as follows: microscopically, no evidence of cell death and detachment was seen; cells did not stain positive for trypan blue; and removal of the inhibitory compound from the culture medium resulted in neurite outgrowth. The compounds tested included GAGs (heparin, dermatan sulfate, chondroitin sulfate A, keratan sulfate and hyaluronic acid), sulfated carbohydrate polymers (dextran sulfate and pentosan polysulfate), and another polyanionic polymer (e.g., alginic acid).

Detailed Description Text (127):
A compound's relative inhibitory potency in vitro appeared to positively correlate with sulfur content. The contribution of the sulfur functional group is most clearly demonstrated by comparing the activity of dextran sulfate to that of dextran. The sulfur found as sulfate on the GAGs most likely affects cell invasion by anionic charge density. To test this hypothesis, we used alginic acid (alginate), a polyanionic polymer with a negative charge due only to carboxyl groups. As shown in Table 10, alginic acid also inhibits cell migration. These results indicate that an active inhibitory element of a given polymer is its anionic (negative) charge density.

☐ 5. Document ID: US 6020326 A

L12: Entry 5 of 9 File: USPT Feb 1, 2000

DOCUMENT-IDENTIFIER: US 6020326 A
TITLE: Method for inhibition of bone growth by anionic polymers

Detailed Description Text (54):
The invention provides for application of an inhibitory composition or inhibitory-adhesive composition by surgical procedures. The inhibitory anionic polymer or inhibitory-adhesive may be applied to a surgical wound. The anionic polymer or inhibitory-adhesive may be directly applied to sites of tissue injury, or to coat an entire organ or to close a surgical incision. Where suitable, administration of the inhibitory anionic polymer or inhibitory-adhesive composition may be made by orthroscopic procedures.

Detailed Description Text (131):
PC-12 cells primed with NGF were plated in 96-well plates. Test solutions were added to the wells and the cells were scored 2 days later as (+) if neurites of at least two cell bodies diameter in length were present on the majority of the cells, and (-) if no or only short processes were present. Complete dose-response curves

were generated for each test compound and the results were expressed as IC.sub.100 (g/ml), i.e., the minimum concentration at which the compound caused 100% inhibition of neurite outgrowth (Table 10). The lack of toxicity by each compound tested was confirmed as follows: microscopically, no evidence of cell death and detachment was seen; cells did not stain positive for trypan blue; and removal of the inhibitory compound from the culture medium resulted in neurite outgrowth. The compounds tested included GAGs heparin, dermatan sulfate, chondroitin sulfate A, keratan sulfate and hyaluronic acid), sulfated carbohydrate polymers (dextran sulfate and pentosan polysulfate), and another polyanionic polymer (e.g., alginic acid).

Detailed Description Text (132):
A compound's relative inhibitory potency in vitro appeared to positively correlate with sulfur content. The contribution of the sulfur functional group is most clearly demonstrated by comparing the activity of dextran sulfate to that of dextran. The sulfur found as sulfate on the GAGs most likely affects cell invasion by anionic charge density. To test this hypothesis, we used alginic acid (alginate), a polyanionic polymer with a negative charge due only to carboxyl groups. As shown in Table 10, alginic acid also inhibits cell migration. These results indicate that an active inhibitory element of a given polymer is its anionic (negative) charge density.

☐ 6. Document ID: US 5994325 A

L12: Entry 6 of 9 File: USPT Nov 30, 1999

DOCUMENT-IDENTIFIER: US 5994325 A
TITLE: Methods and compositions based on inhibition of cell invasion and fibrosis by anionic polymers

Detailed Description Text (53):
The invention provides for application of an inhibitory composition or inhibitory-adhesive composition by surgical procedures. The inhibitory anionic polymer or inhibitory-adhesive may be applied to a surgical wound. The anionic polymer or inhibitory-adhesive may be directly applied to sites of tissue injury, or to coat an entire organ or to close a surgical incision. Where suitable, administration of the inhibitory anionic polymer or inhibitory-adhesive composition may be made by orthroscopic procedures.

Detailed Description Text (123):
PC-12 cells primed with NGF were plated in 96-well plates. Test solutions were added to the wells and the cells were scored 2 days later as (+) if neurites of at least two cell bodies diameter in length were present on the majority of the cells, and (-) if no or only short processes were present. Complete dose-response curves were generated for each test compound and the results were expressed as IC.sub.100 (g/ml), i.e., the minimum concentration at which the compound caused 100% inhibition of neurite outgrowth (Table 10). The lack of toxicity by each compound tested was confirmed as follows: microscopically, no evidence of cell death and detachment was seen; cells did not stain positive for trypan blue; and removal of the inhibitory compound from the culture medium resulted in neurite outgrowth. The compounds tested included GAGs (heparin, dermatan sulfate, chondroitin sulfate A, keratan sulfate and hyaluronic acid), sulfated carbohydrate polymers (dextran sulfate and pentosan polysulfate), and another polyanionic polymer (e.g., alginic

acid).

Detailed Description Text (124):
A compound's relative inhibitory potency in vitro appeared to positively correlate with sulfur content. The contribution of the sulfur functional group is most clearly demonstrated by comparing the activity of dextran sulfate to that of dextran. The sulfur found as sulfate on the GAGs most likely affects cell invasion by anionic charge density. To test this hypothesis, we used alginic acid (alginate), a polyanionic polymer with a negative charge due only to carboxyl groups. As shown in Table 10, alginic acid also inhibits cell migration. These results indicate that an active inhibitory element of a given polymer is its anionic (negative) charge density.

☐ 7. Document ID: US 5705178 A

L12: Entry 7 of 9 File: USPT Jan 6, 1998

DOCUMENT-IDENTIFIER: US 5705178 A
TITLE: Methods and compositions based on inhibition of cell invasion and fibrosis by anionic polymers

Detailed Description Text (55):
The anionic polymers of the present invention are useful in a method of inhibiting the tethering and compression of peripheral nerves which can occur as a result of extraneural scar formation following surgical intervention. This method comprises administering said anionic polymer to the site of the surgical wound. In another embodiment, the inhibitory composition may be used in the treatment of patients with peripheral nerve injury so that the regeneration of nerves may be enhanced by the minimization of scarring, by administering said anionic polymer to the site of peripheral nerve injury.

Detailed Description Text (60):
The invention provides for application of an inhibitory composition or inhibitory-adhesive composition by surgical procedures. The inhibitory anionic polymer or inhibitory-adhesive may be applied to a surgical wound. The anionic polymer or inhibitory-adhesive may be directly applied to sites of tissue injury, or to coat an entire organ or to close a surgical incision. Where suitable, administration of the inhibitory anionic polymer or inhibitory-adhesive composition may be made by orthroscopic procedures.

Detailed Description Text (141):
PC-12 cells primed with NGF were plated in 96-well plates. Test solutions were added to the wells and the cells were scored 2 days later as (+) if neurites of at least two cell bodies diameter in length were present on the majority of the cells, and (-) if no or only short processes were present. Complete dose-response curves were generated for each test compound and the results were expressed as IC.sub.100 (g/ml), i.e., the minimum concentration at which the compound caused 100% inhibition of neurite outgrowth (Table 10). The lack of toxicity by each compound tested was confirmed as follows: microscopically, no evidence of cell death and detachment was seen; cells did not stain positive for trypan blue; and removal of the inhibitory compound from the culture medium resulted in neurite outgrowth. The compounds tested included GAGs (heparin, dermatan sulfate, chondroitin sulfate A, keratan sulfate and hyaluronic acid), sulfated carbohydrate polymers (dextran

sulfate and pentosan polysulfate), and another polyanionic polymer, alginic acid.

Detailed Description Text (142):
A compound's relative inhibitory potency in vitro appeared to positively correlate with sulfur content. The contribution of the sulfur functional group is most clearly demonstrated by comparing the activity of dextran sulfate to that of dextran. The sulfur found as sulfate on the GAGs most likely affects cell invasion by anionic charge density. To test this hypothesis, we used alginic acid (alginate), a polyanionic polymer with a negative charge due only to carboxyl groups. As shown in Table 13, alginic acid also inhibits cell migration. These results indicate that an active inhibitory element of a given polymer is its anionic (negative) charge density.

☐ 8. Document ID: US 5705177 A

L12: Entry 8 of 9 File: USPT Jan 6, 1998

DOCUMENT-IDENTIFIER: US 5705177 A
TITLE: Methods and compositions based on inhibition of cell invasion and fibrosis by anionic polymers

Detailed Description Text (55):
The invention provides for application of an inhibitory composition or inhibitory-adhesive composition by surgical procedures. The inhibitory anionic polymer or inhibitory-adhesive may be applied to a surgical wound. The anionic polymer or inhibitory-adhesive may be directly applied to sites of tissue injury, or to coat an entire organ or to close a surgical incision. Where suitable, administration of the inhibitory anionic polymer or inhibitory-adhesive composition may be made by orthroscopic procedures.

Detailed Description Text (135):
PC-12 cells primed with NGF were plated in 96-well plates. Test solutions were added to the wells and the cells were scored 2 days later as (+) if neurites of at least two cell bodies diameter in length were present on the majority of the cells, and (-) if no or only short processes were present. Complete dose-response curves were generated for each test compound and the results were expressed as IC.sub.100 (g/ml), i.e., the minimum concentration at which the compound caused 100% inhibition of neurite outgrowth (Table 10). The lack of toxicity by each compound tested was confirmed as follows: microscopically, no evidence of cell death and detachment was seen; cells did not stain positive for trypan blue; and removal of the inhibitory compound from the culture medium resulted in neurite Outgrowth. The compounds tested included GAGs (heparin, dermatan sulfate, chondroitin sulfate A, keratan sulfate and hyaluronic acid), sulfated carbohydrate polymers (dextran sulfate and pentosan polysulfate), and another polyanionic polymer (e.g., alginic acid).

Detailed Description Text (136):
A compound's relative inhibitory potency in vitro appeared to positively correlate with sulfur content. The contribution of the sulfur functional group is most clearly demonstrated by comparing the activity of dextran sulfate to that of dextran. The sulfur found as sulfate on the GAGs most likely affects cell invasion by anionic charge density. To test this hypothesis, we used alginic acid (alginate), a polyanionic polymer with a negative charge due only to carboxyl

groups. As shown in Table 13, alginic acid also inhibits cell migration. These results indicate that an active inhibitory element of a given polymer is its anionic (negative) charge density.

☐ 9. Document ID: US 5605938 A

L12: Entry 9 of 9 File: USPT Feb 25, 1997

DOCUMENT-IDENTIFIER: US 5605938 A
TITLE: Methods and compositions for inhibition of cell invasion and fibrosis using dextran sulfate

Detailed Description Text (53):
The invention provides for application of an inhibitory composition or inhibitory-adhesive composition by surgical procedures. The inhibitory anionic polymer or inhibitory-adhesive may be applied to a surgical wound. The anionic polymer or inhibitory-adhesive may be directly applied to sites of tissue injury, or to coat an entire organ or to close a surgical incision. Where suitable, administration of the inhibitory anionic polymer or inhibitory-adhesive composition may be made by orthroscopic procedures.

Detailed Description Text (121):
PC-12 cells primed with NGF were plated in 96-well plates. Test solutions were added to the wells and the cells were scored 2 days later as (+) if neurites of at least two cell bodies diameter in length were present on the majority of the cells, and (-) if no or only short processes were present. Complete dose-response curves were generated for each test compound and the results were expressed as IC.sub.100 (g/ml), i.e., the minimum concentration at which the compound caused 100% inhibition of neurite outgrowth (Table 10). The lack of toxicity by each compound tested was confirmed as follows: microscopically, no evidence of cell death and detachment was seen; cells did not stain positive for trypan blue; and removal of the inhibitory compound from the culture medium resulted in neurite outgrowth. The compounds tested included GAGs (heparin, dermatan sulfate, chondroitin sulfate A, keratan sulfate and hyaluronic acid), sulfated carbohydrate polymers (dextran sulfate and pentosan polysulfate), and another polyanionic polymer (e.g., alginic acid).

Detailed Description Text (122):
A compound's relative inhibitory potency in vitro appeared to positively correlate with sulfur content. The contribution of the sulfur functional group is most clearly demonstrated by comparing the activity of dextran sulfate to that of dextran. The sulfur found as sulfate on the GAGs most likely affects cell invasion by anionic charge density. To test this hypothesis, we used alginic acid (alginate), a polyanionic polymer with a negative charge due only to carboxyl groups. As shown in Table 10, alginic acid also inhibits cell migration. These results indicate that an active inhibitory element of a given polymer is its anionic (negative) charge density.

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